REMARKS/ARGUMENTS

Upon entry of the present Amendment, claim 82 will be pending in the application. Claims 70-81 and 91-92 have been canceled without prejudice. Claim 82 has been rewritten in independent form, incorporating the limitations of canceled base claim 70. No new matter has been introduced by this amendment. Entry of this amendment is respectfully requested.

In the Office Action dated September 11, 2003, the Examiner withdrew the species election requirement presented in the Office Action dated November 1, 2002, and therefore examined all of claims 70-82 and 91-92.

Each of the rejections set forth in the Office Action mailed on September 11, 2003 is addressed individually below. Without acquiescing in the propriety of any of these rejections, in order to expedite prosecution and allowance of this case, claims 70-81 and 91-92 have been canceled, thus rendering many of the rejections moot.

Rejection of Claims 70-82 and 91-92 under 35 U.S.C. § 112, first paragraph

I. Written Description

Claims 70-82 and 91-92 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Examiner opined that the specification does not describe art recognized assays for identifying compounds useful in a composition to reduce skin pigmentation by effecting an alteration in late endosomal/lysosomal trafficking in a skin cell, and for identifying compounds that modulate melanogenesis by affecting P protein function, inhibiting late endosomal/lysosomal trafficking, or inhibiting an ATPase.

Applicants respectfully submit that the specification provides sufficient written description for amended claim 82. Claim 82 recites that the compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell is selected from a particular group of compounds whose chemical structures are provided. Thus, the alleged lack of disclosure of art recognized assays for identifying compounds useful in the claimed compositions is irrelevant, because claim 82 recites particular useful

compounds. The compounds recited in claim 82 are disclosed in the specification, for example, at pages 9-11 and pages 52-53. Thus, the specification clearly provides written description for claim 82.

The written description rejection is moot with respect to claims 70-81 and 91-92, which have been canceled.

Accordingly, Applicants respectfully request that the present written description rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

II. Enablement

Claims 70-82 and 91-92 were also rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner opined that the specification does not enable any and all intended compounds in the claimed compositions. It was asserted that the claims encompass a very large number of compounds, and that the specification does not enable the identification of such a large number of compounds. The Examiner also cited Medline references allegedly teaching that chlorpromazine, a phenothiazine compound intended for use in the claimed compositions, produces skin pigmentation.

Applicants respectfully submit that the specification is enabling for amended claim 82. The Examiner's arguments regarding the need to identify large numbers of compounds and the alleged contradictory teachings with respect to chlorpromazine are inapplicable to claim 82, which recites particular compounds that are disclosed in the specification and do not include chlorpromazine. Indeed, the Examiner has already recognized that the specification is enabling for the particular compounds disclosed in the specification. *See* Office Action of January 27, 2003, page 2, lines 6-7, stating that "the specification, while being enabling for the elected species of claim 73 [a compound of formula (I) recited in part (d) of canceled claim 73], does not reasonably provide enablement for any and all intended compounds of the composition" (emphasis added). Thus, claim 82 is enabled.

The enablement rejection is moot with respect to canceled claims 70-81 and 91-92.

Accordingly, Applicants respectfully submit that the present enablement rejection under 35 U.S.C. § 112, first paragraph, should be reconsidered and withdrawn.

Rejection of Claims 70-82 and 91-92 under 35 U.S.C. § 112, second paragraph

Claims 70-82 and 91-92 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner opined that in claims 70-82 it is not clear whether the term "alteration" is intended to mean inhibit or activate late endosomal/lysosomal trafficking. Applicants respectfully disagree.

The term "alteration" in Applicants' claim 82 clearly refers to a difference in late endosomal/lysosomal trafficking, and need not be limited to activation or inhibition. Indeed, the specification refers to compounds that "alter [*i.e.*, change] or inhibit [*i.e.*, restrain] late endosomal/lysosomal trafficking" (emphasis added) (page 46, lines 4-5 and 10-11) and "methods of inhibiting melanogenesis by altering or inhibiting late endosomal/lysosomal trafficking" (emphasis added) (page 55, lines 19-20 and line 30). Furthermore, the Examiner cited the Webster's II, New Riverside University Dictionary (1984), which defines "alter" as "to make different" or "modify." Thus, the term "alteration" is clear, and need not be limited to inhibition or activation.

Accordingly, claim 82 is definite in reciting "[a] pharmaceutical composition for reducing skin pigmentation, comprising a skin pigmentation reducing effective amount of a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell ... ."

The indefiniteness rejection is moot with respect to canceled claims 70-81.

The Examiner also stated that the phrase "modulates melanogenesis" in claims 91-92 is still confusing. This rejection is moot because claims 91-92 have been canceled.

Accordingly, Applicants respectfully submit that the present rejection under 35 U.S.C. § 112, second paragraph should be reconsidered and withdrawn.

Rejection of Claims 70-81 under 35 U.S.C. § 102(a) and (b)

Claims 70-81 were rejected under 35 U.S.C. § 102(a) and (b) as allegedly being anticipated by various cited references.

These rejections are moot in view of the cancellation of claims 70-81.

Rejection of Claims 70-73 and 82 under 35 U.S.C. § 103(a)

Claims 70-73 and 82 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 3,389,051 to Kagan ("Kagan") in view of CA117:239545.

Applicants' amended claim 82 recites "a pharmaceutical composition for reducing skin pigmentation, comprising a skin pigmentation reducing effective amount of a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell and a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is formulated for topical administration, and wherein the compound that effects the alteration in late endosomal/lysosomal trafficking is selected from the group consisting of [chemical structures]."

Kagan discloses methods for reducing cholesterol in the body by administering particular chemical compounds (col. 1, lines 1-20). The disclosure of Kagan is focused on compositions for oral administration or injection, and does not teach or suggest topical administration of the disclosed cholesterol lowering compositions (*see, e.g.*, col. 4, lines 69-75; col. 5, lines 61-66; Examples 1-8; claims 1-2).

CA117:239545 discloses a transdermal and topical delivery system based on biocompatible polyurethane elastomers. The cited abstract does not teach or suggest the delivery of any particular drug.

To support a *prima facie* case of obviousness, the cited references must teach or suggest every element of the claimed invention, and there must be some suggestion or motivation to combine the teachings of the cited references. The motivation to combine must be found in the prior art, and must not be based on impermissible hindsight in view of Applicants' disclosure. MPEP § 2142.

Neither of the cited references alone teaches or suggests every limitation of Applicants' claim 82. Kagan does not teach or suggest a composition for topical

administration. Thus, the reference does not teach or suggest every limitation of claim 82 either expressly or inherently. CA117:239545 also does not teach or suggest every limitation of claim 82, because the cited abstract does not disclose administration of any of the compounds recited in claim 82. Furthermore, neither reference provides any teaching regarding a topical pharmaceutical composition for reducing skin pigmentation with a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell as claimed.

The Examiner stated that Kagan discloses a compound corresponding to compound VIII of Applicants' claim 82. The Examiner also asserted that Kagan teaches adapting the disclosed compounds for use in suitable forms, so it would have been obvious to deliver a compound disclosed by Kagan in a topical delivery system as disclosed by CA117:239545. However, prior to Applicants' invention, there would have been no motivation to combine the teachings of Kagan, relating to oral or parenteral cholesterol lowering compositions, with the teachings of CA117:239545 directed to a transdermal and topical delivery system. Indeed, Kagan effectively teaches away from the use of transdermal or topical delivery systems such as the one disclosed by CA117:239545.

Kagan discloses a wide range of oral and parenteral formulations for administering the disclosed cholesterol lowering compounds (*see, e.g.*, col. 4, line 69 - col. 5, line 66; Examples 1-8). For example, the passage cited by the Examiner at column 4, lines 70-75 states that "the novel compositions are suitably presented for administration in unit dosage form as tablets, pills, capsules, powders, wafers, cachets, granules, sterile parenteral solutions or suspensions in aqueous or oil vehicles, oral aqueous or oil dispersions, including syrups and elixirs, and the like." However, Kagan does not disclose compositions for topical administration, although the general concept of topical pharmaceutical compositions has been well known for many years. Thus, by disclosing numerous oral and parenteral dosage forms but failing to disclose topical formulations, the teachings of Kagan suggest to one of ordinary skill in the art that the disclosed compositions would not be effective for their intended purpose when

administered topically. Accordingly, there would have been be no motivation to combine the compounds disclosed by Kagan with the topical and transdermal delivery system disclosed in CA117:239545. Indeed, the only possible motivation to combine the cited references would be based on improper hindsight in view of Applicants' disclosure.

Thus, because neither of the cited references alone teaches every limitation of claim 82, and there would have been no motivation to combine the cited references, *prima facie* obviousness has not been established, and claim 82 is not obvious in view of the cited references alone or in combination. The obviousness rejection is moot with respect to claims 70-73, which have been canceled. Accordingly, Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Rejection of Claims 91-92 under 35 U.S.C. § 103(a)

Claims 91-92 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over CA126:190762.

This rejection is moot in view of the cancellation of claims 91-92.

Conclusion

In view of the amendment and arguments set forth herein, Applicants respectfully submit that the rejections contained in the Office Action mailed on September 11, 2003 have been overcome, and that the pending claim is in condition for allowance.

No fees are believed to be due in connection with this correspondence. However, please charge any payments due or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

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